

10/584960

SEQUENCE LISTING **1AP20** Rec'd PCT/PTO 30 JUN 2006

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Lee, Daekee

<120> MODULATION OF EPIDERMAL GROWTH FACTOR HETERODIMER ACTIVITY

<130> 421/99 PCT/US

<150> US 60/545,185

<151> 2004-02-17

<150> PCT/US2005/004968

<151> 2005-02-17

<160> 21

<170> PatentIn version 3.3

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Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
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His Gly Gln Phe Ser Leu Ala Val Val Gly Leu Asn Ile Thr Ser Leu
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Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
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Gly Asn Arg Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
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Phe Gly Thr Pro Asn Gln Lys Thr Lys Ile Met Asn Asn Arg Ala Glu
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Lys Asp Cys Lys Ala Val Asn His Val Cys Asn Pro Leu Cys Ser Ser
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Val Ser Arg Gly Arg Glu Cys Val Glu Lys Cys Asn Ile Leu Glu Gly
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Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
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Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
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Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
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Lys Thr Cys Pro Ala Gly Ile Met Gly Glu Asn Asn Thr Leu Val Trp
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Lys Tyr Ala Asp Ala Asn Asn Val Cys His Leu Cys His Ala Asn Cys
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Thr Tyr Gly Cys Ala Gly Pro Gly Leu Gln Gly Cys Glu Val Trp Pro
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Ser Gly Pro Lys Ile Pro Ser Ile Ala Thr Gly Ile Val Gly Gly Leu
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Leu Phe Ile Val Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg
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Arg His Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg
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Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala
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Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu
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 Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met
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 Thr Ser Thr Val Gln Leu Ile Thr Gln Leu Met Pro Tyr Gly Cys Leu
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 Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg
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 Pro Lys Phe Arg Glu Leu Ile Leu Glu Phe Ser Lys Met Ala Arg Asp
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Pro Gln Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro
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Ser Pro Thr Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp
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 Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
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 Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
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Gln	Arg	Leu	Arg	Ile	Val	Arg	Gly	Thr	Gln	Leu	Phe	Glu	Asp	Asn	Tyr	
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Leu	Cys	Tyr	Gln	Asp	Thr	Ile	Leu	Trp	Lys	Asp	Ile	Phe	His	Lys	Asn	
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Ser	Glu	Asp	Cys	Gln	Ser	Leu	Thr	Arg	Thr	Val	Cys	Ala	Gly	Gly	Cys	
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Ala	Arg	Cys	Lys	Gly	Pro	Leu	Pro	Thr	Asp	Cys	Cys	His	Glu	Gln	Cys	
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gct	gcc	ggc	tgc	acg	ggc	ccc	aag	cac	tct	gac	tgc	ctg	gcc	tgc	ctc	1006
Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys	Leu	
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cac	ttc	aac	cac	agt	ggc	atc	tgt	gag	ctg	cac	tgc	cca	gcc	ctg	gtc	1054
His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu	Val	
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Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu	
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Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu	
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Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp	
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Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu	
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Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln	
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Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys	
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Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
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Glu Asp 1115	Pro Thr Val Pro Leu 1120	Pro Ser Glu Thr Asp 1125	Gly Tyr Val
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Ala Pro 1205	Gln Pro His Pro Pro 1210	Pro Ala Phe Ser Pro 1215	Ala Phe Asp
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 Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
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Ala Ala Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
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Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Leu Arg Lys
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Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu
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Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
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Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
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Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
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Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
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Asn	Pro	Ser	Ser	Gly	Val	Ala	Pro	Leu	Lys	Pro	Glu	His	Leu	Gln	Val	385	390	395	400
Phe	Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp	405	410	415	
Pro	Glu	Ser	Phe	Gln	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Arg	Val	Ile	420	425	430	
Arg	Gly	Arg	Ile	Leu	His	Asp	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly	435	440	445	
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Val	Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His	485	490	495	
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Cys	Arg	Val	Trp	Lys	Gly	Leu	Pro	Arg	Glu	Tyr	Val	Arg	Gly	Lys	His	545	550	555	560
Cys	Leu	Pro	Cys	His	Pro	Glu	Cys	Gln	Pro	Gln	Asn	Ser	Ser	Glu	Thr	565	570	575	
Cys	Tyr	Gly	Ser	Glu	Ala	Asp	Gln	Cys	Glu	Ala	Cys	Ala	His	Tyr	Lys	580	585	590	
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Met Arg Ala Asn Asp Ala Leu Gln Val Leu Gly Leu	
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Leu Phe Ser Leu Ala Arg Gly Ser Glu Val Gly Asn Ser Gln Ala Val	
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Cys Pro Gly Thr Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Glu Asn	
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Gln Tyr Gln Thr Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met	
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His Met Asp Thr Ile Asp Trp Arg Asp Ile Val Arg Asp Arg Asp Ala	
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Leu Thr Lys Thr Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly	
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Cys Ala Gln Cys Ala His Phe Arg Asp Gly Pro His Cys Val Ser Ser	
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Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu
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Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
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Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr
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 Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser
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 His Ala Leu Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser
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 Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
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 Lys Asp Asn Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly
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 Arg Cys Trp Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr
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 Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn
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 Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
 225 230 235 240
 Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
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 Cys Pro Pro Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys
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Glu Pro Cys Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser
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Gly Ser Arg Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val
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Asn Cys Thr Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu
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Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln
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Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
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Thr Ile Gly Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile
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Met Lys Asn Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu
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His His Ser Leu Asn Trp Thr Lys Val Leu Arg Gly Pro Thr Glu Glu
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Arg Leu Asp Ile Lys His Asn Arg Pro Arg Arg Asp Cys Val Ala Glu
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Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Gly Gly Val
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Val Leu Gly Ala Lys Gly Pro Ile Tyr Lys Tyr Pro Asp Val Gln Asn
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Glu Leu Gln Asp Cys Leu Gly Gln Thr Leu Val Leu Ile Gly Lys Thr
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His Leu Thr Met Ala Leu Thr Val Ile Ala Gly Leu Val Val Ile Phe
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Met Met Leu Gly Gly Thr Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln
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Asn Lys Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu
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Pro Leu Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe
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Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe
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Gly Thr Val His Lys Gly Val Trp Ile Pro Glu Gly Glu Ser Ile Lys
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Ile Pro Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser
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Phe Gln Ala Val Thr Asp His Met Leu Ala Ile Gly Ser Leu Asp His
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Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln
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 945 950 955 960
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 980 985 990
 His Gly Leu Thr Asn Lys Lys Leu Glu Glu Val Glu Leu Glu Pro Glu
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1070						1075					1080			
Leu	His	Pro	Met	Pro	Arg	Gly	Cys	Leu	Ala	Ser	Glu	Ser	Ser	Glu
1085						1090					1095			
Gly	His	Val	Thr	Gly	Ser	Glu	Ala	Glu	Leu	Gln	Glu	Lys	Val	Ser
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Asp	Ser	Ala	Tyr	His	Ser	Gln	Arg	His	Ser	Leu	Leu	Thr	Pro	Val
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Thr	Pro	Leu	Ser	Pro	Pro	Gly	Leu	Glu	Glu	Glu	Asp	Val	Asn	Gly
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Tyr	Val	Met	Pro	Asp	Thr	His	Leu	Lys	Gly	Thr	Pro	Ser	Ser	Arg
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Ala Phe Gln Gly Pro Gly His Gln Ala Pro His Val His Tyr Ala
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 Ala Arg Gly Ser Glu Met Gly Asn Ser Gln Ala Val Cys Pro Gly Thr
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 cta aac ggg ctg agt gtg acc ggc gat gct gac aac cag tac cag aca 144
 Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Asp Asn Gln Tyr Gln Thr
 35 40 45
 ctg tac aaa ctc tat gag aag tgt gag gtg gtc atg ggt aac ctg gag 192
 Leu Tyr Lys Leu Tyr Glu Lys Cys Glu Val Val Met Gly Asn Leu Glu
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 Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
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 cga gaa gtg aca ggc tat gta ctg gtg gcc atg aat gaa ttc tct gta 288
 Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Val
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ctg ccc tta cct aac ctc cga gtg gtc cgg gga acc cag gtc tac gat	336
Leu Pro Leu Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp	
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Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser	
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His Ala Leu Arg Gln Leu Arg Phe Thr Gln Leu Thr Glu Ile Leu Leu	
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Lys Asn Asn Gly Gly Asn Cys Pro Pro Cys His Glu Val Cys Lys Gly	
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cga tgc tgg ggg cct gga cca gaa gac tgc cag ata ttg acc aag acc	624
Arg Cys Trp Gly Pro Gly Pro Glu Asp Cys Gln Ile Leu Thr Lys Thr	
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Ile Cys Ala Pro Gln Cys Asn Gly Arg Cys Phe Gly Pro Asn Pro Asn	
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Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp	
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Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val	
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Pro Arg Cys Pro Ala Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu	
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Glu Pro Asn Pro His Ile Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala	
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Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Phe Cys Val Arg Ala	
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Cys Pro Ala Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys	
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Glu Pro Cys Arg Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser	
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Gly Ser Arg Tyr Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val	
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Asn Gly Asp Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu	
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Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln	
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Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr	
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Thr Ile Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile	
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Cys Val Thr His Cys Asn Val Leu Gln Gly Glu Pro Arg Glu Phe Val	
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Glu Leu Gln Asp Cys Leu Gly Gln Ala Glu Val Leu Met Ser Lys Pro	
625 630 635 640	
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His Leu Val Ile Ala Val Thr Val Gly Leu Thr Val Ile Phe Leu Ile	
645 650 655	
ctg gga ggc tct ttt ctc tat tgg cgt gga cgc agg att cag aat aaa	2016
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Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe Lys Glu	
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Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe Gly Thr	
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Val His Lys Gly Ile Trp Ile Pro Glu Gly Glu Ser Ile Lys Ile Pro	
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Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser Phe Gln	
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Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln Leu Val	
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Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg Gln His	
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Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Ser Met Val His Arg Asp	
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Lys Arg Ala Ser Gly Pro Gly Ile Pro Pro Ala Ala Glu Pro Ser Ala	
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Tyr His Ser Gln Arg His Ser Leu Leu Thr Pro Val Thr Pro Leu	
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cgt ggt gcg ggc ggt tcc gga ggg gat tat gca gct atg ggg gcc	3834
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Cys Pro Ala Ala Glu Gln Gly Tyr Glu Glu Met Arg Ala Phe Gln	
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Gly Pro Gly His Gln Ala Pro His Val Arg Tyr Ala Arg Leu Lys	
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Thr Leu Arg Ser Leu Glu Ala Thr Asp Ser Ala Phe Asp Asn Pro	
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Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser	
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His Ala Leu Arg Gln Leu Arg Phe Thr Gln Leu Thr Glu Ile Leu Leu
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Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
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Lys Asn Asn Gly Gly Asn Cys Pro Pro Cys His Glu Val Cys Lys Gly
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Ile Cys Ala Pro Gln Cys Asn Gly Arg Cys Phe Gly Pro Asn Pro Asn
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Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
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Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
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Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
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Gly Lys Val Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro
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Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Glu Gly Val
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 690 695 700

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Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser Phe Gln
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Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly
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Ser	Arg	Ser	Arg	Ser	Arg	Ser	Pro	Arg	Pro	Arg	Gly	Asp	Ser	Ala
1115						1120					1125			
Tyr	His	Ser	Gln	Arg	His	Ser	Leu	Leu	Thr	Pro	Val	Thr	Pro	Leu
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 Trp Val Trp Val Ser Leu Leu Val Ala Ala Gly Thr Val Gln Pro Ser
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 Asp Ser Gln Ser Val Cys Ala Gly Thr Glu Asn Lys Leu Ser Ser Leu
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 Ser Asp Leu Glu Gln Gln Tyr Arg Ala Leu Arg Lys Tyr Tyr Glu Asn
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 Cys Glu Val Val Met Gly Asn Leu Glu Ile Thr Ser Ile Glu His Asn
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 Arg Asp Leu Ser Phe Leu Arg Ser Val Arg Glu Val Thr Gly Tyr Val
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 Ile Ile Arg Gly Thr Lys Leu Tyr Glu Asp Arg Tyr Ala Leu Ala Ile
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Leu Lys Asn Leu Thr Glu Ile Leu Asn Gly Gly Val Tyr Val Asp Gln	
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Asn Lys Phe Leu Cys Tyr Ala Asp Thr Ile His Trp Gln Asp Ile Val	
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Ser Gly Cys Gly Arg Cys His Lys Ser Cys Thr Gly Arg Cys Trp Gly	
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ccc aca gaa aat cat tgc cag act ttg aca agg acg gtg tgt gca gaa	678
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Gln Cys Asp Gly Arg Cys Tyr Gly Pro Tyr Val Ser Asp Cys Cys His	
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Gln Thr Phe Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe	
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Asp Ile Cys Pro Lys Ala Cys Asp Gly Ile Gly Thr Gly Ser Leu Met	
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Thr Lys Ile Asn Gly Asn Leu Ile Phe Leu Val Thr Gly Ile His Gly	
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Lys Asp Gly Pro Asn Cys Val Glu Lys Cys Pro Asp Gly Leu Gln Gly	
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Asp Cys Ile Tyr Tyr Pro Trp Thr Gly His Ser Thr Leu Pro Gln His	
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Lys Ala Asn Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met	
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Asp His Pro His Leu Val Arg Leu Leu Gly Val Cys Leu Ser Pro Thr	
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 980 985 990

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 Phe Phe Gln Asn Leu Leu Asp Glu Glu Asp Leu Glu Asp Met Met Asp
 995 1000 1005

gct gag gaa tat ttg gtc ccc cag gct ttc aac ata cct cct ccc Ala Glu Glu Tyr Leu Val Pro Gln Ala Phe Asn Ile Pro Pro Pro 1010 1015 1020	3069
atc tac aca tcc aga aca aga att gac tcc aat agg agt gaa att Ile Tyr Thr Ser Arg Thr Arg Ile Asp Ser Asn Arg Ser Glu Ile 1025 1030 1035	3114
gga cac agc cct cct cct gcc tac acc ccc atg tcg gga aat cag Gly His Ser Pro Pro Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln 1040 1045 1050	3159
ttt gtg tac caa gat ggg ggc ttt gct aca caa caa gga atg ccc Phe Val Tyr Gln Asp Gly Gly Phe Ala Thr Gln Gln Gly Met Pro 1055 1060 1065	3204
atg ccc tac aga gcc aca acc agc acc ata cca gag gct cca gta Met Pro Tyr Arg Ala Thr Thr Ser Thr Ile Pro Glu Ala Pro Val 1070 1075 1080	3249
gct cag ggt gca acg gct gag atg ttt gat gac tcc tgc tgt aat Ala Gln Gly Ala Thr Ala Glu Met Phe Asp Asp Ser Cys Cys Asn 1085 1090 1095	3294
ggt acc cta cga aag cca gtg gca ccc cat gtc caa gag gac agt Gly Thr Leu Arg Lys Pro Val Ala Pro His Val Gln Glu Asp Ser 1100 1105 1110	3339
agc act cag agg tat agt gct gat ccc aca gtg ttc gcc cca gaa Ser Thr Gln Arg Tyr Ser Ala Asp Pro Thr Val Phe Ala Pro Glu 1115 1120 1125	3384
cgg aat cct cga gga gaa ctg gat gaa gaa ggc tac atg act cca Arg Asn Pro Arg Gly Glu Leu Asp Glu Glu Gly Tyr Met Thr Pro 1130 1135 1140	3429
atg cat gac aag ccc aaa caa gaa tat ctg aat cct gtg gaa gag Met His Asp Lys Pro Lys Gln Glu Tyr Leu Asn Pro Val Glu Glu 1145 1150 1155	3474
aac cct ttt gtg tcc cga agg aag aat gga gat ctt caa gct tta Asn Pro Phe Val Ser Arg Arg Lys Asn Gly Asp Leu Gln Ala Leu 1160 1165 1170	3519
gat aat ccg gag tat cac agt gct tcc agc ggt cca ccc aag gcg Asp Asn Pro Glu Tyr His Ser Ala Ser Ser Gly Pro Pro Lys Ala 1175 1180 1185	3564
gag gat gaa tac gtg aat gag cct cta tac ctc aac acc ttc gcc Glu Asp Glu Tyr Val Asn Glu Pro Leu Tyr Leu Asn Thr Phe Ala 1190 1195 1200	3609
aat gcc ttg ggg agt gca gag tac atg aaa aac agt gta ctg tct Asn Ala Leu Gly Ser Ala Glu Tyr Met Lys Asn Ser Val Leu Ser 1205 1210 1215	3654
gtg cca gag aaa gcc aag aaa gca ttt gac aac ccc gac tac tgg Val Pro Glu Lys Ala Lys Lys Ala Phe Asp Asn Pro Asp Tyr Trp 1220 1225 1230	3699

aac cac agc ctg cca ccc cgg agc acc ctt cag cac cca gac tac 3744
 Asn His Ser Leu Pro Pro Arg Ser Thr Leu Gln His Pro Asp Tyr
 1235 1240 1245
 ctg cag gaa tac agc aca aaa tat ttt tat aaa cag aat gga cgg 3789
 Leu Gln Glu Tyr Ser Thr Lys Tyr Phe Tyr Lys Gln Asn Gly Arg
 1250 1255 1260
 atc cgc ccc att gtg gca gag aat cct gag tac ctc tcg gag ttc 3834
 Ile Arg Pro Ile Val Ala Glu Asn Pro Glu Tyr Leu Ser Glu Phe
 1265 1270 1275
 tcg ctg aag cct ggc act atg ctg ccc cct ccg ccc tac aga cac 3879
 Ser Leu Lys Pro Gly Thr Met Leu Pro Pro Pro Pro Tyr Arg His
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 cgg aat act gtg gtg tga 3897
 Arg Asn Thr Val Val
 1295

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 <211> 1298
 <212> PRT
 <213> Mus musculus

<400> 21

Met Ala Ile Pro Ser Arg Arg Lys Asp Tyr Pro Lys Leu Ser Glu Ile
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Thr Val Cys Ala Gly Thr Glu Asn Lys Leu Ser Ser Leu Ser Asp Leu
 20 25 30

Glu Gln Gln Tyr Arg Ala Leu Arg Lys Tyr Tyr Glu Asn Cys Glu Val
 35 40 45

Val Met Gly Asn Leu Glu Ile Thr Ser Ile Glu His Asn Arg Asp Leu
 50 55 60

Ser Phe Leu Arg Ser Ile Arg Glu Val Thr Gly Tyr Val Leu Val Ala
 65 70 75 80

Leu Asn Gln Phe Arg Tyr Leu Pro Leu Glu Asn Leu Arg Ile Ile Arg
 85 90 95

Gly Thr Lys Leu Tyr Glu Asp Arg Tyr Ala Leu Ala Ile Phe Leu Asn
 100 105 110

Tyr Arg Lys Asp Gly Asn Phe Gly Leu Gln Glu Leu Gly Leu Lys Asn
 115 120 125

Leu Thr Glu Ile Leu Asn Gly Gly Val Tyr Val Asp Gln Asn Lys Phe
 130 135 140

Leu Cys Tyr Ala Asp Thr Ile His Trp Gln Asp Ile Val Arg Asn Pro
 145 150 155 160

Trp Pro Ser Asn Met Thr Leu Val Ser Thr Asn Gly Ser Ser Gly Cys
 165 170 175

Gly Arg Cys His Lys Ser Cys Thr Gly Arg Cys Trp Gly Pro Thr Glu
 180 185 190

Asn His Cys Gln Thr Leu Thr Arg Thr Val Cys Ala Glu Gln Cys Asp
 195 200 205

Gly Arg Cys Tyr Gly Pro Tyr Val Ser Asp Cys Cys His Arg Glu Cys
 210 215 220

Ala Gly Gly Cys Ser Gly Pro Lys Asp Thr Asp Cys Phe Ala Cys Met
 225 230 235 240

Asn Phe Asn Asp Ser Gly Ala Cys Val Thr Gln Cys Pro Gln Thr Phe
 245 250 255

Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe Asn Ala Lys
 260 265 270

Tyr Thr Tyr Gly Ala Phe Cys Val Lys Lys Cys Pro His Asn Phe Val
 275 280 285

Val Asp Ser Ser Ser Cys Val Arg Ala Cys Pro Ser Ser Lys Met Glu
 290 295 300

Val Glu Glu Asn Gly Ile Lys Met Cys Lys Pro Cys Thr Asp Ile Cys
 305 310 315 320

Pro Lys Ala Cys Asp Gly Ile Gly Thr Gly Ser Leu Met Ser Ala Gln
 325 330 335

Thr Val Asp Ser Ser Asn Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile
 340 345 350

Asn Gly Asn Leu Ile Phe Leu Val Thr Gly Ile His Gly Asp Pro Tyr
 355 360 365

Asn Ala Ile Asp Ala Ile Asp Pro Glu Lys Leu Asn Val Phe Arg Thr
 370 375 380

Val Arg Glu Ile Thr Gly Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn
 385 390 395 400

Met Thr Asp Phe Ser Val Phe Ser Asn Leu Val Thr Ile Gly Gly Arg
 405 410 415

Val Leu Tyr Ser Gly Leu Ser Leu Leu Ile Leu Lys Gln Gln Gly Ile
 420 425 430

Thr Ser Leu Gln Phe Gln Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile
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Tyr Ile Thr Asp Asn Ser Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp
 450 455 460

Thr Thr Leu Phe Ser Thr Ile Asn Gln Arg Ile Val Ile Arg Asp Asn
 465 470 475 480

Arg Arg Ala Glu Asn Cys Thr Ala Glu Gly Met Val Cys Asn His Leu
 485 490 495

Cys Ser Asn Asp Gly Cys Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser
 500 505 510

Cys Arg Arg Phe Ser Arg Gly Lys Ile Cys Ile Glu Ser Cys Asn Leu
 515 520 525

Tyr Asp Gly Glu Phe Arg Glu Phe Glu Asn Gly Ser Ile Cys Val Glu
 530 535 540

Cys Asp Ser Gln Cys Glu Lys Met Glu Asp Gly Leu Leu Thr Cys His
 545 550 555 560

Gly Pro Gly Pro Asp Asn Cys Thr Lys Cys Ser His Phe Lys Asp Gly
 565 570 575

Pro Asn Cys Val Glu Lys Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser
 580 585 590

Phe Ile Phe Lys Tyr Ala Asp Gln Asp Arg Glu Cys His Pro Cys His
 595 600 605

Pro Asn Cys Thr Gln Gly Cys Asn Gly Pro Thr Ser His Asp Cys Ile
 610 615 620

Tyr Tyr Pro Trp Thr Gly His Ser Thr Leu Pro Gln His Ala Arg Thr
 625 630 635 640

Pro Leu Ile Ala Ala Gly Val Ile Gly Gly Leu Phe Ile Leu Val Ile
 645 650 655

Met Ala Leu Thr Phe Ala Val Tyr Val Arg Arg Lys Ser Ile Lys Lys
 660 665 670

Lys Arg Ala Leu Arg Arg Phe Leu Glu Thr Glu Leu Val Glu Pro Leu
 675 680 685

Thr Pro Ser Gly Thr Ala Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys
 690 695 700

Glu Thr Glu Leu Lys Arg Val Lys Val Leu Gly Ser Gly Ala Phe Gly
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Thr Val Tyr Lys Gly Ile Trp Val Pro Glu Gly Glu Thr Val Lys Ile
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Pro Val Ala Ile Lys Ile Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn
 740 745 750

Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met Asp His Pro
 755 760 765

His Leu Val Arg Leu Leu Gly Val Cys Leu Ser Pro Thr Ile Gln Leu
 770 775 780

Val Thr Gln Leu Met Pro His Gly Cys Leu Leu Asp Tyr Val His Glu
 785 790 795 800

His Lys Asp Asn Ile Gly Ser Gln Leu Leu Leu Asn Trp Cys Val Gln
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Ile Ala Lys Gly Met Met Tyr Leu Glu Glu Arg Arg Leu Val His Arg
 820 825 830

Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys
 835 840 845

Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu
 850 855 860

Tyr Asn Ala Asp Gly Gly Lys Met Pro Ile Lys Trp Met Ala Leu Glu
 865 870 875 880

Cys Ile His Tyr Arg Lys Phe Thr His Gln Ser Asp Val Trp Ser Tyr
 885 890 895

Gly Val Thr Ile Trp Glu Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp
 900 905 910

Gly Ile Pro Thr Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg
 915 920 925

Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Val Met Val
 930 935 940

Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu
 945 950 955 960

Ala Ala Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Tyr Leu Val
 965 970 975

Ile Gln Gly Asp Asp Arg Met Lys Leu Pro Ser Pro Asn Asp Ser Lys
 980 985 990

Phe Phe Gln Asn Leu Leu Asp Glu Glu Asp Leu Glu Asp Met Met Asp
 995 1000 1005

Ala Glu Glu Tyr Leu Val Pro Gln Ala Phe Asn Ile Pro Pro Pro
 1010 1015 1020

Ile Tyr Thr Ser Arg Thr Arg Ile Asp Ser Asn Arg Ser Glu Ile
 1025 1030 1035

Gly His Ser Pro Pro Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln
 1040 1045 1050

Phe Val Tyr Gln Asp Gly Gly Phe Ala Thr Gln Gln Gly Met Pro
 1055 1060 1065

Met Pro Tyr Arg Ala Thr Thr Ser Thr Ile Pro Glu Ala Pro Val
 1070 1075 1080

Ala	Gln	Gly	Ala	Thr	Ala	Glu	Met	Phe	Asp	Asp	Ser	Cys	Cys	Asn
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Gly	Thr	Leu	Arg	Lys	Pro	Val	Ala	Pro	His	Val	Gln	Glu	Asp	Ser
1100						1105					1110			
Ser	Thr	Gln	Arg	Tyr	Ser	Ala	Asp	Pro	Thr	Val	Phe	Ala	Pro	Glu
1115						1120					1125			
Arg	Asn	Pro	Arg	Gly	Glu	Leu	Asp	Glu	Glu	Gly	Tyr	Met	Thr	Pro
1130						1135					1140			
Met	His	Asp	Lys	Pro	Lys	Gln	Glu	Tyr	Leu	Asn	Pro	Val	Glu	Glu
1145						1150					1155			
Asn	Pro	Phe	Val	Ser	Arg	Arg	Lys	Asn	Gly	Asp	Leu	Gln	Ala	Leu
1160						1165					1170			
Asp	Asn	Pro	Glu	Tyr	His	Ser	Ala	Ser	Ser	Gly	Pro	Pro	Lys	Ala
1175						1180					1185			
Glu	Asp	Glu	Tyr	Val	Asn	Glu	Pro	Leu	Tyr	Leu	Asn	Thr	Phe	Ala
1190						1195					1200			
Asn	Ala	Leu	Gly	Ser	Ala	Glu	Tyr	Met	Lys	Asn	Ser	Val	Leu	Ser
1205						1210					1215			
Val	Pro	Glu	Lys	Ala	Lys	Lys	Ala	Phe	Asp	Asn	Pro	Asp	Tyr	Trp
1220						1225					1230			
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1235						1240					1245			
Leu	Gln	Glu	Tyr	Ser	Thr	Lys	Tyr	Phe	Tyr	Lys	Gln	Asn	Gly	Arg
1250						1255					1260			
Ile	Arg	Pro	Ile	Val	Ala	Glu	Asn	Pro	Glu	Tyr	Leu	Ser	Glu	Phe
1265						1270					1275			
Ser	Leu	Lys	Pro	Gly	Thr	Met	Leu	Pro	Pro	Pro	Pro	Tyr	Arg	His
1280						1285					1290			
Arg	Asn	Thr	Val	Val										
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